

07/838675
5/10/95

(FILE 'USPAT' ENTERED AT 09:52:03 ON 10 MAY 95)

L1 870 S HYALURONAT? OR HYALURONIC?
L2 645759 S TREAT? OR ADMINIST? OR DELIVER?
L3 55 S L1 (5A) L2

=> d cit bib ab 1-55

1. 5,411,743, May 2, 1995, Prevention of synovial adhesions; Larry J. Moore, et al., 424/450; 514/825 [IMAGE AVAILABLE]

US PAT NO: 5,411,743 [IMAGE AVAILABLE] L3: 1 of 55 DATE ISSUED: May 2, 1995
TITLE: Prevention of synovial adhesions
INVENTOR: Larry J. Moore, Altadena, CA
Jill Adler-Moore, Altadena, CA
ASSIGNEE: Vestar, Inc., San Dimas, CA (U.S. corp.)
APPL-NO: 08/157,841
DATE FILED: Nov. 23, 1993
ART-UNIT: 152
PRIM-EXMR: Gollamudi S. Kishore
LEGAL-REP: Adam Cochran, George A. Gilbert

US PAT NO: 5,411,743 [IMAGE AVAILABLE] L3: 1 of 55

ABSTRACT:

Adhesions in synovial capsules are prevented through the administration of liposome intercalated nonsteroidal anti-inflammatory agents.

2. 5,366,958, Nov. 22, 1994, Localized delivery using fibronectin conjugates; Alan L. Weiner, et al., 514/2; 424/450; 530/380, 810, 812 [IMAGE AVAILABLE]

US PAT NO: 5,366,958 [IMAGE AVAILABLE] L3: 2 of 55 DATE ISSUED: Nov. 22, 1994
TITLE: Localized delivery using fibronectin conjugates INVENTOR: Alan L. Weiner, Plainsboro, NJ
Robert P. Lenk, Lambertville, NJ
Sharon S. Carpenter-Green, Cranbury, NJ
Michael W. Fountain, Plainsboro, NJ

ASSIGNEE: The Liposome Company, Inc., Princeton, NJ (U.S. corp.) APPL-NO: 08/110,193
DATE FILED: Aug. 20, 1993
ART-UNIT: 184
PRIM-EXMR: Jacqueline Stone
LEGAL-REP: Allen Bloom, Joanne Longo Feeney

US PAT NO: 5,366,958 [IMAGE AVAILABLE] L3: 2 of 55

ABSTRACT:

This invention encompasses new and substantially improved methods and compositions for delivery of therapeutic agents to specifically chosen body sites. Conjugation of fibronectin to bioactive agents or to lipids or to liposomes which entrap the bioactive agents permits immobilization of the bioactive agent when **administered** at collagen-, heparin-, **hyaluronic** acid-, fibrin/fibrinogen-, or ganglioside-rich sites. Covalent conjugation is achieved by two methods: (1) the enzymatically catalyzed cross-linkage of fibronectin to an amine containing compound, and (2) by a modified NHS method which permits formation of peptide bonds between fibronectin and lipid compounds.

3. 5,364,845, Nov. 15, 1994, Glucosamine, chondroitin and manganese composition for the protection and repair of connective tissue; Robert W. Henderson, 514/54, 62 [IMAGE AVAILABLE]

US PAT NO: 5,364,845 [IMAGE AVAILABLE] L3: 3 of 55 DATE ISSUED: Nov. 15, 1994
TITLE: Glucosamine, chondroitin and manganese composition for the protection and repair of connective tissue
INVENTOR: Robert W. Henderson, Baldwin
ASSIGNEE: Nutramax Laboratories, Inc., Baltimore, MD (U.S. corp.) APPL-NO: 08/040,936
DATE FILED: Mar. 31, 1993
ART-UNIT: 125
PRIM-EXMR: Marianne M. Cintins
ASST-EXMR: T. J. Criares
LEGAL-REP: Leonard Bloom

US PAT NO: 5,364,845 [IMAGE AVAILABLE] L3: 3 of 55

ABSTRACT:

A therapeutic composition for the protection, treatment and repair of connective tissue in mammals and a method for the treatment of connective tissue in mammals by the administration of the composition. The composition includes glucosamine and preferably chondroitin sulfate. The composition further includes manganese ascorbate which catalyzes the production of collagen and proteoglycans from the glucosamine and the chondroitin sulfate.

4. 5,358,706, Oct. 25, 1994, Muco-adhesive polymers; Lawrence Marlin, et al., 424/78.04, 427; 514/912, 915 [IMAGE AVAILABLE]

✓ US PAT NO: 5,358,706 [IMAGE AVAILABLE] L3: 4 of 55 DATE ISSUED: Oct. 25, 1994
TITLE: Muco-adhesive polymers
INVENTOR: Lawrence Marlin, Bridgewater, NJ
Ronald K. Yamamoto, San Francisco, CA
ASSIGNEE: Union Carbide Chemicals & Plastics Technology Corporation, Danbury, CT (U.S. corp.)
APPL-NO: 07/954,753
DATE FILED: Sep. 30, 1992
ART-UNIT: 152
PRIM-EXMR: Thurman K. Page
ASST-EXMR: Peter F. Kulkosky
LEGAL-REP: W. K. Volles

US PAT NO: 5,358,706 [IMAGE AVAILABLE] L3: 4 of 55
ABSTRACT:
Cationic polysaccharide polymers and anionic therapeutic agents delivery systems are disclosed which have been found to be substantive to mucosal surfaces. The present delivery system is well suited for the delivery of anionic ophthalmic pharmaceuticals.

5. 5,356,883, Oct. 18, 1994, Water-insoluble derivatives of hyaluronic acid and their methods of preparation and use; Jing-Wen Kuo, et al., 514/54; 424/7.1, 488; 514/777; 536/4.1 [IMAGE AVAILABLE]

✓ US PAT NO: 5,356,883 [IMAGE AVAILABLE] L3: 5 of 55 DATE ISSUED: Oct. 18, 1994
TITLE: Water-insoluble derivatives of hyaluronic acid and their methods of preparation and use
INVENTOR: Jing-Wen Kuo, Stoneham, MA
David A. Swann, Lexington, MA
Glenn D. Prestwich, Harbor, NY
ASSIGNEE: Research Foundation of State University of N.Y., Albany, NY (U.S. corp.)
Anika Research, Inc., Woburn, MA (U.S. corp.) APPL-NO: 07/920,698
DATE FILED: Jul. 28, 1992
ART-UNIT: 188
PRIM-EXMR: Douglas W. Robinson
ASST-EXMR: Francisco Prats
LEGAL-REP: Hamilton, Brook, Smith & Reynolds

US PAT NO: 5,356,883 [IMAGE AVAILABLE] L3: 5 of 55
ABSTRACT:
This invention describes a method for preparing water-insoluble biocompatible gels, films and sponges by reacting hyaluronic acid, or a salt thereof, with a carbodiimide in the absence of a nucleophile or a polyanionic polysaccharide. The water-insoluble gels, films and sponges of this invention may be used as surgical aids to prevent adhesions of body tissues and as drug delivery vehicles.

6. 5,336,767, Aug. 9, 1994, Total or partial esters of hyaluronic acid; Francesco della Valle, et al., 536/55.1; 424/443 [IMAGE AVAILABLE]

✓ US PAT NO: 5,336,767 [IMAGE AVAILABLE] L3: 6 of 55 DATE ISSUED: Aug. 9, 1994
TITLE: Total or partial esters of hyaluronic acid
INVENTOR: Francesco della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy
ASSIGNEE: Fidia, S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 07/998,749
DATE FILED: Dec. 30, 1992
ART-UNIT: 152
PRIM-EXMR: Thurman K. Page
ASST-EXMR: R. Harrison
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 5,336,767 [IMAGE AVAILABLE] L3: 6 of 55

ABSTRACT:

The invention concerns the esters of hyaluronic acid in which all or only a portion of the carboxylic groups of the acid are esterified, and the salts of the partial esters with metals or with pharmacologically acceptable organic bases. The compounds possess interesting and precious bioplastic and pharmaceutical properties and may be used in innumerable fields, including cosmetics, surgery and medicine. The invention also includes pharmaceutical preparations containing, as an active ingredient, one or more hyaluronic acid esters, or a salt thereof as described above, as well as medicaments containing:

- 1) a pharmacologically active substance or an association of pharmacologically active substances and
- 2) a carrying vehicle containing a total or partial ester of hyaluronic acid. The invention includes also various uses of the hyaluronic esters or of the above mentioned medicaments, such as in medicine, surgery or cosmetics. The invention relates to a new procedure for the preparation of polysaccharide esters containing carboxylic groups, such as in particular the above mentioned hyaluronic acid esters

7. 5,316,926, May 31, 1994, Method for the microbiological production of non-antigenic hyaluronic acid; Karen K. Brown, et al., 435/101, 172.1, 253.4, 885; 536/55.1, 124 [IMAGE AVAILABLE]

✓
US PAT NO: 5,316,926 [IMAGE AVAILABLE] L3: 7 of 55 DATE ISSUED: May 31, 1994
TITLE: Method for the microbiological production of non-antigenic hyaluronic acid
INVENTOR: Karen K. Brown, Parkville, MO
Linda L. C. Ruiz, Haneohe, HI
Ivo van de Rijn, Winston-Salem, NC
Nathan D. Greene, Leawood, KS
Sandy L. Trump, De Soto, KS
Curtis D. Wilson, Shawnee Mission, KS
Sharon A. Bryant, Shawnee, KS
ASSIGNEE: Miles Inc., Pittsburgh, PA (U.S. corp.)
APPL-NO: 07/796,178
DATE FILED: Nov. 22, 1991
ART-UNIT: 188
PRIM-EXMR: Irene Marx
LEGAL-REP: Joseph C. Gil, Lyndanne M. Whalen

US PAT NO: 5,316,926 [IMAGE AVAILABLE] L3: 7 of 55
ABSTRACT:

The present disclosure is concerned with the production of high molecular weight **hyaluronic** acid suitable for medicinal **administration** to mammals without provoking an immune response from microbiological fermentation. The cultures may be prepared from specially developed strains of hyaluronic acid generating bacteria obtained by passaging in serologically negative host animal blood. The cultures are kept in log phase growth for an extended period by appropriate temperature, pH and glucose content adjustments. If the cultured strain is not hyaluronidase negative the hyaluronidase activity is inhibited. The hyaluronic acid is precipitated from the culture by the sequential addition of an anionic surfactant and then a cationic surfactant and extended from the precipitate with a high molarity aqueous calcium ion solution. The isolated aqueous hyaluronic acid solution may then be purified by passage through a nitrocellulose filter. Its pyrogenicity may be alleviated by treatment with a strong acid washed activated carbon.

8. 5,263,992, Nov. 23, 1993, Biocompatible device with covalently bonded biocompatible agent; Patrick E. Guire, 623/66; 436/501; 604/266; 623/1, 11, 12 [IMAGE AVAILABLE]

US PAT NO: 5,263,992 [IMAGE AVAILABLE] L3: 8 of 55 DATE ISSUED: Nov. 23, 1993
TITLE: Biocompatible device with covalently bonded biocompatible agent
INVENTOR: Patrick E. Guire, Eden Prairie, MN
ASSIGNEE: Bio-Metric Systems, Inc., Eden Prairie, MN (U.S. corp.) APPL-NO: 07/783,711
DATE FILED: Oct. 24, 1991
ART-UNIT: 338
PRIM-EXMR: David Isabella
ASST-EXMR: Paul Prebille
LEGAL-REP: Fredrikson & Byron

US PAT NO: 5,263,992 [IMAGE AVAILABLE] L3: 8 of 55
ABSTRACT:

The biocompatibility of biomaterials having solid surfaces is improved through coating the same with biocompatible agents. The method for modifying the solid surface to improve biocompatibility employs molecules of a biocompatible agent and a chemical linking moiety possessing a photochemically reactive group capable upon activation of covalently bonding to the solid surface and possessing a different reactive group as capable upon activation of covalently bonding to separate molecules of the biocompatible agent. One of the groups is unresponsive to activation by a stimulus to which the other group is responsive. The method

comprises applying stimulus to sequentially activate the groups and covalently bind the different reactive group of the linking moiety to the molecules of the biocompatible agent and to photochemically covalently bind the linking moiety to the solid surface with a sufficient population density to enable the molecules of the biocompatible agent to effectively shield the solid surface and to provide a biocompatible surface.

9. 5,234,914, Aug. 10, 1993, Methods of treating hemorrhoids and anorectal disease; Damian J. Gallina, 514/54; 424/489; 514/882, 912, 944, 966; 536/18.7, 54, 55.1, 55.3 [IMAGE AVAILABLE]

US PAT NO: 5,234,914 [IMAGE AVAILABLE] L3: 9 of 55 DATE ISSUED: Aug. 10, 1993
TITLE: Methods of treating hemorrhoids and anorectal disease INVENTOR: Damian J. Gallina, Erie, PA
ASSIGNEE: Patent Biopharmaceutics, Inc., Erie, PA (U.S. corp.) APPL-NO: 07/799,751
DATE FILED: Nov. 27, 1991
ART-UNIT: 185
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Louis N. Leary
LEGAL-REP: Cushman, Darby & Cushman

US PAT NO: 5,234,914 [IMAGE AVAILABLE] L3: 9 of 55
ABSTRACT:

A method of treating hemorrhoids and anorectal disease which includes applying to the hemorrhoids and anorectal tissues an effective amount of a composition including a pharmaceutically acceptable carrier and hyaluronic acid or pharmaceutically acceptable salts thereof.

10. 5,229,127, Jul. 20, 1993, Rapid miosis with control of intraocular pressure using a mixture of a cetylcholine and carbachol derivatives; James W. McKinzie, 424/427; 215/231, 263, 265, 294, 301, DIG.3; 424/422; 514/912, 913 [IMAGE AVAILABLE]

US PAT NO: 5,229,127 [IMAGE AVAILABLE] L3: 10 of 55 DATE ISSUED: Jul. 20, 1993
TITLE: Rapid miosis with control of intraocular pressure using a mixture of a cetylcholine and carbachol derivatives INVENTOR: James W. McKinzie, 3124 Solimar Beach Dr., Ventura, CA 93001
APPL-NO: 07/621,082
DATE FILED: Dec. 3, 1990
ART-UNIT: 152
PRIM-EXMR: Thurman K. Page
ASST-EXMR: E. J. Webman
LEGAL-REP: Marvin E. Jacobs

US PAT NO: 5,229,127 [IMAGE AVAILABLE] L3: 10 of 55
ABSTRACT:

Quick miosis with 24 hour control of intraocular pressure of patients undergoing extracapsular cataract extraction surgery is achieved by applying to the eyes of the patient during surgery acetylcholine as a first miotic agent and carbachol as a second miotic agent. Acetylcholine provides quick miosis while carbachol enhances the miotic effect while providing post-surgery control of intraocular pressure. The two miotic agents can be dissolved in a common saline carrier. The two agents can be combined in a unit dosage package by disposing acetylcholine in powder form in a first compartment and a solution of carbachol in a second compartment. The combined miotic agent of the invention is especially useful when substances which raise IOP such as viscoelastic agents are used during ocular surgery and/or with sensitive patients who enter the surgery with elevated pressure such as those suffering from glaucoma.

11. 5,219,360, Jun. 15, 1993, Mammary prosthesis fill and method of making same; Nicholas G. Georgiade, 623/8, 11 [IMAGE AVAILABLE]

US PAT NO: 5,219,360 [IMAGE AVAILABLE] L3: 11 of 55 DATE ISSUED: Jun. 15, 1993
TITLE: Mammary prosthesis fill and method of making same INVENTOR: Nicholas G. Georgiade, Durham, NC
ASSIGNEE: Fortis Research Corporation, Durham, NC (U.S. corp.) APPL-NO: 07/698,302
DATE FILED: May 10, 1991
ART-UNIT: 338
PRIM-EXMR: David Isabella
LEGAL-REP: Olive & Olive PA

US PAT NO: 5,219,360 [IMAGE AVAILABLE] L3: 11 of 55
ABSTRACT:

A surgical mammary prosthesis containing a liquid-gel of cross-linked hyaluronic acid (hylan) inside a medical grade elastomer, and a method of making a prosthesis containing such a liquid-gel. Because the gel used in the invention contains a nontoxic, nonantigenic, noninflammatory, biodegradable natural substance, problems attributed to or associated with previous silicone gel filled prostheses as a result of prosthesis rupture or leakage or "bleed" are avoided.

✓ 12. 5,202,431, Apr. 13, 1993, Partial esters of hyaluronic acid; Francesco della Valle, et al., 536/55.1; 424/423, 489 [IMAGE AVAILABLE]

US PAT NO: 5,202,431 [IMAGE AVAILABLE] L3: 12 of 55 DATE ISSUED: Apr. 13, 1993
TITLE: Partial esters of hyaluronic acid
INVENTOR: Francesco della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy
ASSIGNEE: Fidia, S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 07/794,703
DATE FILED: Nov. 20, 1991
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 5,202,431 [IMAGE AVAILABLE] L3: 12 of 55
ABSTRACT:

The invention concerns the esters of hyaluronic acid in which all or only a portion of the carboxylic groups of the acid are esterified, and the salts of the partial esters with metals or with pharmacologically acceptable organic bases. The compounds possess interesting and precious bioplastic and pharmaceutical properties and may be used in innumerable fields, including cosmetics, surgery and medicine. The invention also includes pharmaceutical preparations containing, as an active ingredient, one or more hyaluronic acid esters, or a salt thereof as described above, as well as medicaments containing:

- 1) a pharmacologically active substance or an association of pharmacologically active substances and
- 2) a carrying vehicle containing a total or partial ester of hyaluronic acid. The invention includes also various uses of the hyaluronic esters or of the above mentioned medicaments, such as in medicine, surgery or cosmetics.

The invention also relates to a new procedure for the preparation of polysaccharide esters containing carboxylic groups, such as in particular the above mentioned hyaluronic acid esters.

13. 5,177,105, Jan. 5, 1993, Methods for controlling intraocular pressure with transition metal complexes; Hans R. Moll, et al., 514/502, 913 [IMAGE AVAILABLE]

US PAT NO: 5,177,105 [IMAGE AVAILABLE] L3: 13 of 55 DATE ISSUED: Jan. 5, 1993
TITLE: Methods for controlling intraocular pressure with transition metal complexes
INVENTOR: Hans R. Moll, Weatherford, TX
Mark T. DuPriest, Fort Worth, TX
ASSIGNEE: Alcon Laboratories, Inc., Fort Worth, TX (U.S. corp.) APPL-NO: 07/823,082
DATE FILED: Jan. 14, 1992
ART-UNIT: 125
PRIM-EXMR: Frederick E. Waddell
ASST-EXMR: Zohreh A. Fay
LEGAL-REP: James A. Arno, Sally S. Yeager

US PAT NO: 5,177,105 [IMAGE AVAILABLE] L3: 13 of 55
ABSTRACT:

Methods for lowering elevated intraocular pressure resulting from the instillation to the eye of sodium **hyaluronate** during surgery by **administration** of transition metal complexes are disclosed.

14. 5,166,331, Nov. 24, 1992, Hyaluronics acid fractions, methods for the preparation thereof, and pharmaceutical compositions containing same; Francesco della Valle, et al., 536/55.1; 424/78.05; 514/54, 420, 576, 777, 912 [IMAGE AVAILABLE]

✓ US PAT NO: 5,166,331 [IMAGE AVAILABLE] L3: 14 of 55 DATE ISSUED: Nov. 24, 1992
TITLE: Hyaluronics acid fractions, methods for the preparation thereof, and pharmaceutical compositions containing same
INVENTOR: Francesco della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy
Silvana Lorenzi, Padova, Italy
ASSIGNEE: Fidia, S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 07/452,681
DATE FILED: Dec. 19, 1989
ART-UNIT: 153
PRIM-EXMR: Nathan M. Nutter
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 5,166,331 [IMAGE AVAILABLE] L3: 14 of 55
ABSTRACT:

Two pharmaceutically useful fractions of hyaluronic acid are obtained comprising a first fraction with a molecular weight between 50,000 and 100,000 which is useful for wound healing, and a second fraction having a molecular weight between 500,000 and 730,000 which is useful for intraocular and intraarticular injections.

In addition, pharmaceutical preparations for topical administration are provided containing a pharmacologically active substance together with hyaluronic acid or a molecular weight fraction thereof. The hyaluronic acid may be in the form of the free acid or may be a salt with an alkali or alkaline earth metal, magnesium, aluminum or ammonium, or in the form of a salt with one or more pharmacologically active substances.

15. 5,145,841, Sep. 8, 1992, Anti-inflammatory compounds and compositions; David Cullis-Hill, et al., 514/54; 536/21, 54, 55.1, 121 [IMAGE AVAILABLE]

US PAT NO: 5,145,841 [IMAGE AVAILABLE] L3: 15 of 55 DATE ISSUED: Sep. 8, 1992
TITLE: Anti-inflammatory compounds and compositions INVENTOR: David Cullis-Hill, Bondi Junction, Australia
Peter Ghosh, Fairlight, Australia
ASSIGNEE: Arthroparm PTY. Limited, NSW, Australia (foreign corp.) APPL-NO: 07/423,455
DATE FILED: Sep. 19, 1989
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Nancy S. Carson
LEGAL-REP: Nixon & Vanderhye

US PAT NO: 5,145,841 [IMAGE AVAILABLE] L3: 15 of 55
ABSTRACT:

Method for the treatment of arthritis, rheumatism and inflammation of connective tissue in which a multivalent metal ion substantially pure complex of xylan polysulphate, wherein the multivalent metal ion is selected from the group consisting of Ca.sup.2+, Mg.sup.2+, Cu.sup.2+ and Zn.sup.2+ is administered to a patient in need of such treatment.

16. 5,137,875, Aug. 11, 1992, Hyaluronic acid-containing aqueous solution or aqueous dispersion of collagen; Makoto Tsunenaga, et al., 514/21; 530/356 [IMAGE AVAILABLE]

US PAT NO: 5,137,875 [IMAGE AVAILABLE] L3: 16 of 55 DATE ISSUED: Aug. 11, 1992
TITLE: Hyaluronic acid-containing aqueous solution or aqueous dispersion of collagen
INVENTOR: Makoto Tsunenaga, Yokohama, Japan
Naoki Tominaga, Yokohama, Japan
Toshio Nishiyama, Tokyo, Japan
Toru Yamashita, Yokohama, Japan
Mutsumi Fukuyama, Kawagoe, Japan
Teruo Miyata, Tokyo, Japan
Masayasu Furuse, Sagamihara, Japan
ASSIGNEE: Shiseido Co., Ltd., Tokyo, Japan (foreign corp.) Koken Co., Ltd., Tokyo, Japan (foreign corp.)
APPL-NO: 07/339,765
DATE FILED: Apr. 18, 1989
ART-UNIT: 181
PRIM-EXMR: Howard E. Schain
ASST-EXMR: Choon P. Koh
LEGAL-REP: Varndell Legal Group

US PAT NO: 5,137,875 [IMAGE AVAILABLE] L3: 16 of 55
ABSTRACT:

A hyaluronic acid-containing aqueous solution or aqueous dispersion of collagen having a pH of from about 6.5 to about 8.0 and an osmolality of from about 230 to about 320 mOsm/kgH.sub.2 O. The aqueous solution or the aqueous dispersion of collagen is useful as an agent for correction and reparation of a depressed part of or a void in soft tissue of mammals.

17. 5,128,326, Jul. 7, 1992, Drug delivery systems based on hyaluronans derivatives thereof and their salts and methods of producing same; Endre A. Balazs, et al., 514/54; 424/446; 514/769 [IMAGE AVAILABLE]

US PAT NO: 5,128,326 [IMAGE AVAILABLE] L3: 17 of 55 DATE ISSUED: Jul. 7, 1992
TITLE: Drug delivery systems based on hyaluronans derivatives thereof and their salts and methods of producing same INVENTOR: Endre A. Balazs, Ft. Lee, NJ
Adolf Leshchiner, Fairview, NJ
Nancy E. Larsen, Ridgely Park, NJ
ASSIGNEE: Biomatrix, Inc., Ridgely Park, NJ (U.S. corp.) APPL-NO: 07/559,413
DATE FILED: Jul. 23, 1990
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Sheldon Palmer

US PAT NO: 5,128,326 [IMAGE AVAILABLE] L3: 17 of 55

ABSTRACT:

Disclosed are drug delivery systems based on a polymeric component which is soluble or insoluble (cross-linked) hyaluronan or hyaluronan copolymerized with another hydrophilic polymer or hylan and one or more substances having biological or pharmacological activity and methods of preparing same.

✓ 18. 5,099,013, Mar. 24, 1992, Hylan preparation and method of recovery thereof from animal tissues; Endre A. Balazs, et al., 536/55.1; 435/267 [IMAGE AVAILABLE]

US PAT NO: 5,099,013 [IMAGE AVAILABLE] L3: 18 of 55 DATE ISSUED: Mar. 24, 1992

TITLE: Hylan preparation and method of recovery thereof from animal tissues

INVENTOR: Endre A. Balazs, Ft. Lee, NJ

Adolf Leshchiner, Fairview, NJ

Adelya Leshchiner, Fairview, NJ

Nancy Larsen, Southfield, NY

Philip Band, Brooklyn, NY

ASSIGNEE: Biomatrix, Inc., Ridgefield, NJ (U.S. corp.) APPL-NO: 07/616,706

DATE FILED: Nov. 16, 1990

ART-UNIT: 183

PRIM-EXMR: Ronald W. Griffin

LEGAL-REP: Sheldon Palmer

US PAT NO: 5,099,013 [IMAGE AVAILABLE] L3: 18 of 55

ABSTRACT:

Disclosed is hylan, a chemically modified hyaluronan preparation characterized by the presence of small amounts (0.0002-0.05% by weight) of aldehyde cross-linking groups covalently bonded to the hyaluronan molecular chains. Also disclosed is an improved method of obtaining hylan comprising treating hyaluronan in situ in animal tissues containing same with a treatment mixture including an aldehyde which is reactive towards hyaluronic acid and the proteins contained in the animal tissue. Treatment is effected at temperatures below about 16.degree. C. at very high pH, e.g., 8-14 whereby the overall yield is increased while maintaining the high molecular weight of the hylan.

19. 5,095,037, Mar. 10, 1992, Combined anti-inflammatory agent; Kenichi Iwamitsu, et al., 514/561 [IMAGE AVAILABLE]

✓ US PAT NO: 5,095,037 [IMAGE AVAILABLE] L3: 19 of 55 DATE ISSUED: Mar. 10, 1992

TITLE: Combined anti-inflammatory agent

INVENTOR: Kenichi Iwamitsu, Kobe, Japan

Yukio Nakamura, Nara, Japan

Masahiro Kawasaki, Kashiwara, Japan

Yoshio Fukui, Ibaraki, Japan

ASSIGNEE: Nissho Corporation, Osaka, Japan (foreign corp.) APPL-NO: 07/623,318

DATE FILED: Dec. 6, 1990

ART-UNIT: 125

PRIM-EXMR: Stanley J. Friedman

LEGAL-REP: Varndell Legal Group

US PAT NO: 5,095,037 [IMAGE AVAILABLE] L3: 19 of 55

ABSTRACT:

A pharmaceutical composition for treating inflammatory diseases, comprising (A) an effective amount of hyaluronic acid or its salt, and (B) an effective amount of an anti-inflammatory agent. The composition exhibits a synergistic therapeutic effect on inflammations and is useful for treating inflammatory diseases, particularly diseases of joint with inflammation.

20. 5,093,487, Mar. 3, 1992, Low viscosity high molecular weight filter sterilizable hyaluronic acid; Karen K. Brown, et al., 536/55.1, 124, 127 [IMAGE AVAILABLE]

✓ US PAT NO: 5,093,487 [IMAGE AVAILABLE] L3: 20 of 55 DATE ISSUED: Mar. 3, 1992

TITLE: Low viscosity high molecular weight filter sterilizable hyaluronic acid

INVENTOR: Karen K. Brown, Kansas City, MO

Nathan D. Greene, Leawood, KS

Sandy L. Trump, DeSoto, KS

Sharon A. Bryant, Shawnee, KS

ASSIGNEE: Mobay Corporation, Pittsburgh, PA (U.S. corp.) APPL-NO: 06/816,548

DATE FILED: Jan. 6, 1986

ART-UNIT: 183

PRIM-EXMR: Johnnie R. Brown
ASST-EXMR: Elli Peselev
LEGAL-REP: Joseph C. Gil, Lyndanne M. Whalen

US PAT NO: 5,093,487 [IMAGE AVAILABLE] L3: 20 of 55

ABSTRACT:

The present disclosure is concerned with procedures for adjusting the average molecular weight, the molecular weight distribution and the viscosity in solution of hyaluronic acid and its salts (HA), particularly its sodium and potassium salts. The average molecular weight can be increased and the molecular weight distribution can be narrowed by precipitating this material into a bath of a non-solvent containing a continuously moving device to which it can adhere as it precipitates. The solution viscosity of this or any high molecular weight, high viscosity HA can be reduced without substantially effecting its molecular weight by either a moderate temperature heat treatment or passage through a fine (one micron or less) pore filter as a one weight percent or stronger aqueous solution. The disclosure is also concerned with the high molecular weight low solution viscosity HA so obtained.

21. 5,079,236, Jan. 7, 1992, Pure, sterile, pyrogen-free hyaluronic acid formulations their methods of preparation and methods of use; Alan Drizen, et al., 514/54; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 5,079,236 [IMAGE AVAILABLE] L3: 21 of 55 DATE ISSUED: Jan. 7, 1992

TITLE: Pure, sterile, pyrogen-free hyaluronic acid formulations their methods of preparation and methods of use

INVENTOR: Alan Drizen, Downsview, Canada
Anita Aviad, Toronto, Canada

ASSIGNEE: Hyal Pharmaceutical Corporation, Mississauga, Canada (foreign corp.)

APPL-NO: 07/054,859

DATE FILED: May 27, 1987

ART-UNIT: 183

PRIM-EXMR: John W. Rollins

ASST-EXMR: Elli Peselev

LEGAL-REP: Roper & Quigg

US PAT NO: 5,079,236 [IMAGE AVAILABLE] L3: 21 of 55

ABSTRACT:

A heat stable, purified, pyrogen-free, heat sterilized fraction of hyaluronic acid suitable for use in formulations for intra-articular treatment of animals which includes minor amounts of sulphated mucopolysaccharides, sulphated ash, chlorides, solvents and less than 0.6% protein, having a molecular weight of less than 750,000 and exhibiting a specific absorbance of a 1% solution at A257nm of less than 3. A formulation for intra-articular treatment of animals including an aqueous solution of the heat stable fraction of hyaluronic acid and preservatives, such as sodium benzoate, methylparaben and propylparaben, having a pH of 6.8-8.0 at 25.degree. C. A method of preparing a formulation for intra-articular treatment of animals involving adding and dissolving methyl parahydroxybenzoate, propyl parahydroxybenzoate and sodium benzoate in hot water, mixing the preservative solution to dissolve the parabens, adding sodium hyaluronate in the solution, adjusting the pH of the resultant solution to 6.8-8.0 and diluting with water to a final volume prior to filling suitable dosages for intra-articular treatment of animals into vials which are autoclaved to sterilize the aqueous formulation. An intra-articular treatment involving injecting a suitable dosage of an aqueous solution containing a heat stable, purified, pyrogen-free, heat-sterilized fraction of hyaluronic acid into a joint of an animal suffering from a degenerative joint disease.

22. 5,073,545, Dec. 17, 1991, Agent containing an ellagic acid series compound for external application and use thereof; Masatoshi Arima, et al., 514/27; 424/195.1; 514/53, 453 [IMAGE AVAILABLE]

US PAT NO: 5,073,545 [IMAGE AVAILABLE] L3: 22 of 55 DATE ISSUED: Dec. 17, 1991

TITLE: Agent containing an ellagic acid series compound for external application and use thereof

INVENTOR: Masatoshi Arima, Odawara, Japan
Hiroaki Nishizawa, Fujisawa, Japan
Keiji Takeuchi, Tokyo, Japan
Hiroshi Deura, Yotsukaidou, Japan
Keiichiro Ishida, Tokyo, Japan

ASSIGNEE: Lion Corporation, Tokyo, Japan (foreign corp.) APPL-NO: 07/202,321

DATE FILED: Jun. 6, 1988

ART-UNIT: 183

PRIM-EXMR: Johnnie R. Brown

ASST-EXMR: Elli Peselev

LEGAL-REP: Burns, Doane, Swecker & Mathis

US PAT NO: 5,073,545 [IMAGE AVAILABLE] L3: 22 of 55

ABSTRACT:

Agents for external application contain as an effective component ellagic acid series compounds represented by the general formula [I] or salts thereof: ##STR1## wherein R.sub.1 to R.sub.4 are a hydrogen atom, an alkyl group having 1 to 20 carbon atoms, an alkoxy group having 1 to 20 carbon atoms, a polyalkylene oxide residue where the alkylene oxide unit has 2 to 3 carbon atoms, or a sugar residue represented by the formula [II]: ##STR2## and R.sub.5 is a hydrogen atom, a hydroxyl group or an alkoxy group having 1 to 8 carbon atoms.

23. 5,019,498, May 28, 1991, Method of assaying high molecular hyaluronic acid and kit of reagents for such assay; Kenji Chichibu, 435/7.5, 7.9, 7.94, 975; 436/501, 518, 524, 527, 529, 808, 815 [IMAGE AVAILABLE]

US PAT NO: 5,019,498 [IMAGE AVAILABLE] L3: 23 of 55 DATE ISSUED: May 28, 1991
TITLE: Method of assaying high molecular hyaluronic acid and kit of reagents for such assay
INVENTOR: Kenji Chichibu, Saitama, Japan
ASSIGNEE: Chugai Seiyaku Kabushiki Kaisha, Tokyo, Japan (foreign corp.)
APPL-NO: 07/162,672
DATE FILED: Mar. 1, 1988
ART-UNIT: 182
PRIM-EXMR: Esther L. Kepplinger
ASST-EXMR: Toni R. Scheiner
LEGAL-REP: Browdy and Neimark

US PAT NO: 5,019,498 [IMAGE AVAILABLE] L3: 23 of 55
ABSTRACT:

A high molecular hyaluronic acid which is an important factor in the diagnosis of inflammations such as rheumatism or diseases such as cancer is assayed as a complex of sandwich structure in which a hyaluronic acid binding protein is coupled to the hyaluronic acid of interest at two or more sites of binding without the need to employ a competitive reaction as in the prior art techniques of assay. The assay method of the present invention does not require a purified form of hyaluronic acid as a reagent and permits as small as 10 ng of a high molecular hyaluronic acid to be detected or quantified by a very simple operation.

24. 5,009,892, Apr. 23, 1991, Rapid miosis with control of intraocular pressure; James W. McKinzie, 424/422, 423, 427, 428 [IMAGE AVAILABLE]

US PAT NO: 5,009,892 [IMAGE AVAILABLE] L3: 24 of 55 DATE ISSUED: Apr. 23, 1991
TITLE: Rapid miosis with control of intraocular pressure INVENTOR: James W. McKinzie, 3124 Solimar Beach Dr.,
Ventura, CA 93001
APPL-NO: 07/318,753
DATE FILED: Mar. 3, 1989
ART-UNIT: 152
PRIM-EXMR: Thurman K. Page
LEGAL-REP: Marvin E. Jacobs

US PAT NO: 5,009,892 [IMAGE AVAILABLE] L3: 24 of 55
ABSTRACT:

Quick miosis with 24 hour control of intraocular pressure of patients undergoing extracapsular cataract extraction surgery is achieved by applying to the eyes of the patient during surgery acetylcholine as a first miotic agent and carbachol as a second miotic agent. Acetylcholine provides quick miosis while carbachol enhances the miotic effect while providing post-surgery control of intraocular pressure. The two miotic agents can be dissolved in a common saline carrier. The two agents can be combined in a unit dosage package by disposing acetylcholine in powder form in a first compartment and a solution of carbachol in a second compartment. The combined miotic agent of the invention is especially useful when substances which raise IOP such as viscoelastic agents are used during ocular surgery and/or with sensitive patients who enter the surgery with elevated pressure such as those suffering from glaucoma.

25. 4,979,959, Dec. 25, 1990, Biocompatible coating for solid surfaces; Patrick E. Guire, 623/66; 351/160H; 435/176, 180; 623/1, 6, 11 [IMAGE AVAILABLE]

US PAT NO: 4,979,959 [IMAGE AVAILABLE] L3: 25 of 55 DATE ISSUED: Dec. 25, 1990
TITLE: Biocompatible coating for solid surfaces
INVENTOR: Patrick E. Guire, Eden Prairie, MN
ASSIGNEE: Bio-Metric Systems, Inc., Eden Prairie, MN (U.S. corp.) APPL-NO: 07/349,884
DATE FILED: May 5, 1989
ART-UNIT: 338
PRIM-EXMR: Randall L. Green
ASST-EXMR: Paul Prebilic
LEGAL-REP: James R. Haller, Mary P. Bauman, Gregory P. Kaihoi

US PAT NO: 4,979,959 [IMAGE AVAILABLE] L3: 25 of 55

ABSTRACT:

The biocompatibility of biomaterials having solid surfaces is improved through coating the same with biocompatible agents where the biocompatible agents are covalently bonded to the solid surface via a chemical linking moiety. The method for modifying the solid surface to improve biocompatibility employs molecules of a biocompatible agent and a chemical linking moiety possessing a photochemically reactive group capable upon activation of covalently bonding to the solid surface and possessing a different reactive group as capable upon activation of covalently bonding to separate molecules of the biocompatible agent. One of the groups is unresponsive to activation by a stimulus to which the other group is responsive. The method comprises applying stimulus to sequentially activate the groups and covalently bind the different reactive group of the linking moiety to the molecules of the biocompatible agent and to photochemically covalently bind the linking moiety to the solid surface with a sufficient population density to enable the molecules of the biocompatible agent to effectively shield the solid surface and to provide a biocompatible surface.

26. 4,973,493, Nov. 27, 1990, Method of improving the biocompatibility of solid surfaces; Patrick E. Guire, 427/2.24, 2.1, 2.25, 2.26, 2.3; 435/181; 436/905; 623/66, 901 [IMAGE AVAILABLE]

US PAT NO: 4,973,493 [IMAGE AVAILABLE] L3: 26 of 55 DATE ISSUED: Nov. 27, 1990
TITLE: Method of improving the biocompatibility of solid surfaces INVENTOR: Patrick E. Guire, Eden Prairie, MN
ASSIGNEE: Bio-Metric Systems, Inc., Eden Prairie, MN (U.S. corp.) APPL-NO: 07/108,765
DATE FILED: Oct. 15, 1987
ART-UNIT: 338
PRIM-EXMR: Randall L. Green
ASST-EXMR: Paul Prebilit
LEGAL-REP: James R. Bauman, Mary P. Haller, Gregory P. Kaihoi
US PAT NO: 4,973,493 [IMAGE AVAILABLE] L3: 26 of 55
ABSTRACT:

A method for modifying the solid surface to improve its biocompatibility is disclosed. The method employs molecules of a biocompatible agent and a chemical linking moiety possessing a photochemically reactive group capable upon activation of covalently bonding to the solid surface and possessing a different reactive group as capable upon activation of covalently bonding to separate molecules of the biocompatible agent. The method comprises applying stimulus to sequentially activate the groups and covalently bind the different reactive group of the linking moiety to the molecules of the biocompatible agent and to photochemically covalently bind the linking moiety to the solid surface with a sufficient population density to enable the molecules of the biocompatible agent to effectively shield the solid surface and to provide a biocompatible surface.

27. 4,970,298, Nov. 13, 1990, Biodegradable matrix and methods for producing same; Frederick H. Silver, et al., 530/356; 128/DIG.8; 424/94.64, 485; 523/105, 111 [IMAGE AVAILABLE]

US PAT NO: 4,970,298 [IMAGE AVAILABLE] L3: 27 of 55 DATE ISSUED: Nov. 13, 1990
TITLE: Biodegradable matrix and methods for producing same INVENTOR: Frederick H. Silver, Long Valley, NJ
Richard A. Berg, Lambertville, NJ
Charles J. Doillon, Edison, NJ
Kevin Weadock, Piscataway, NJ
Conrad Whyne, Edgewood, MD
ASSIGNEE: University of Medicine and Dentistry of New Jersey, Newark, NJ (U.S. corp.)
APPL-NO: 06/875,827
DATE FILED: Jun. 18, 1986
ART-UNIT: 153
PRIM-EXMR: John Kight
ASST-EXMR: Nathan M. Nutter
LEGAL-REP: Weiser & Stapler

US PAT NO: 4,970,298 [IMAGE AVAILABLE] L3: 27 of 55

ABSTRACT:

This invention relates to a biodegradable collagen matrix having a pore size and morphology which enhances the healing of a wound. It further relates to a process for preparing the matrix. One embodiment of the invention comprises a biodegradable matrix which comprises collagen, hyaluronic acid and fibronectin. Other embodiments include a process which comprises freeze drying a dispersion containing collagen, crosslinking the collagen via two crosslinking steps and freeze drying the crosslinked matrix.

28. 4,965,353, Oct. 23, 1990, Polysaccharide esters and their salts; Francesco della Valle, et al., 536/55.1; 424/423, 443, 489, 490; 514/54, 969 [IMAGE AVAILABLE]

US PAT NO: 4,965,353 [IMAGE AVAILABLE] L3: 28 of 55 DATE ISSUED: Oct. 23, 1990

TITLE: Polysaccharide esters and their salts
INVENTOR: Francesco della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy
ASSIGNEE: Fidia S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 07/339,919
DATE FILED: Apr. 19, 1989
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 4,965,353 [IMAGE AVAILABLE] L3: 28 of 55

ABSTRACT:

The invention concerns the esters of hyaluronic acid in which all or only a portion of the carboxylic groups of the acid are esterified, and the salts of the partial esters with metals or with pharmacologically acceptable organic bases.

The compounds possess interesting and precious bioplastic and pharmaceutical properties and may be used in innumerable fields, including cosmetics, surgery and medicine. The invention also includes pharmaceutical preparations containing, as an active ingredient, one or more hyaluronic acid esters, or a salt thereof as described above, as well as medicaments containing: (1) a pharmacologically active substance or an association of pharmacologically active substances and (2) a carrying vehicle containing a total or partial ester of hyaluronic acid.

The invention includes also various uses of the hyaluronic esters or of the above mentioned medicaments, such as in medicine, surgery or cosmetics.

The invention also relates to a new procedure for the preparation of polysaccharide esters containing carboxylic groups, such as in particular the above mentioned hyaluronic acid esters.

29. 4,957,744, Sep. 18, 1990, Cross-linked esters of hyaluronic acid; Francesco della Valle, et al., 424/401, 423, 443, 451, 489; 512/5; 514/54, 844, 880; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 4,957,744 [IMAGE AVAILABLE] L3: 29 of 55 DATE ISSUED: Sep. 18, 1990

TITLE: Cross-linked esters of hyaluronic acid
INVENTOR: Francesco della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy

ASSIGNEE: Fidia, S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 07/106,658
DATE FILED: Oct. 13, 1987
ART-UNIT: 183
PRIM-EXMR: John W. Rollins
ASST-EXMR: Elli Pescelev
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 4,957,744 [IMAGE AVAILABLE] L3: 29 of 55

ABSTRACT:

Cross-linked esters of hyaluronic acid are provided which result from the esterification of polyhydric alcohols with two or more carboxy groups of the hyaluronic acid polysaccharide. These cross-linked esters are useful in the field of biodegradable plastics for sanitary and surgical articles and in the pharmaceutical and cosmetic fields for the preparation of useful compositions and articles.

30. 4,946,780, Aug. 7, 1990, Method for producing sodium hyaluronate by fermentation method; Masamichi Hashimoto, et al., 435/101, 885 [IMAGE AVAILABLE]

US PAT NO: 4,946,780 [IMAGE AVAILABLE] L3: 30 of 55 DATE ISSUED: Aug. 7, 1990

TITLE: Method for producing sodium hyaluronate by fermentation method
INVENTOR: Masamichi Hashimoto, Tokyo, Japan
Haruhisa Saegusa, Yokohama, Japan
Susumu Chiba, Machida, Japan
Hironoshin Kitagawa, Machida, Japan
Teruzo Miyoshi, Yokohama, Japan

ASSIGNEE: Denki Kagaku Kogyo Kabushiki Kaisha, Tokyo, Japan (foreign corp.)
APPL-NO: 07/347,337
DATE FILED: May 4, 1989
ART-UNIT: 188
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Pamela S. Webber
LEGAL-REP: Keil & Weinkauff

US PAT NO: 4,946,780 [IMAGE AVAILABLE] L3: 30 of 55

ABSTRACT:

A method for producing sodium hyaluronate by a fermentation method comprises culturing a mutant strain FM 100 derived from *Streptococcus equi* and partially free from auxotrophy to thereby stably produce sodium hyaluronate and accumulating the hyaluronate. A method for producing sodium hyaluronate by a fermentation method comprises culturing a mutant strain FM 300 derived from *Streptococcus equi* and partially free from auxotrophy to thereby stably produce sodium hyaluronate and accumulating the hyaluronate.

31. 4,940,751, Jul. 10, 1990, Wettable silicon elastomer for the manufacture of contact lenses; Jean-Marc Frances, et al., 525/54.2; 264/331.11, 340; 525/54.21, 54.24, 474, 476, 478 [IMAGE AVAILABLE]

US PAT NO: 4,940,751 [IMAGE AVAILABLE] L3: 31 of 55 DATE ISSUED: Jul. 10, 1990
TITLE: Wettable silicon elastomer for the manufacture of contact lenses
INVENTOR: Jean-Marc Frances, Vcilleurbanne, France
Georges Wajs, Ivry sur Seine, France
ASSIGNEE: Essilor International (Compagnie Generale d'Optique), Creteil, France (foreign corp.)
APPL-NO: 07/261,790
DATE FILED: Oct. 24, 1988
ART-UNIT: 151
PRIM-EXMR: Melvyn I. Marquis
LEGAL-REP: Felfe & Lynch

US PAT NO: 4,940,751 [IMAGE AVAILABLE] L3: 31 of 55

ABSTRACT:

The wettable silicone elastomer is obtained by crosslinking of a composition of epoxidized silicones. The elastomer thus obtained is made wettable by grafting saccharide compounds on epoxy groups of the elastomer. The invention is applied in particular to the manufacture of contact lenses.

32. 4,920,104, Apr. 24, 1990, Sodium hyaluronate composition; Dale P. DeVore, et al., 514/54, 55, 912 [IMAGE AVAILABLE]

US PAT NO: 4,920,104 [IMAGE AVAILABLE] L3: 32 of 55 DATE ISSUED: Apr. 24, 1990
TITLE: Sodium hyaluronate composition
INVENTOR: Dale P. DeVore, Chelmsford, MA
David A. Swann, Lexington, MA
Bernard P. Sullivan, Andover, MA
ASSIGNEE: MedChem Products, Inc., Acton, MA (U.S. corp.) APPL-NO: 07/194,187
DATE FILED: May 16, 1988
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Pamela S. Webber
LEGAL-REP: Kane, Dalsimer, Sullivan, Kurucz, Levy, Eisele and Richard
US PAT NO: 4,920,104 [IMAGE AVAILABLE] L3: 32 of 55

ABSTRACT:

Solutions of sodium hyaluronate in physiological saline with a kinematic viscosity of from 45,000 to 64,000 cSt. are found to effect a smaller increase in post-operative intra-ocular pressure following use as an aid in ophthalmological surgery, when the weight average molecular weight of the hyaluronate is within the range of from 1 to 2 million Daltons.

33. 4,886,787, Dec. 12, 1989, Method of preventing adhesion between body tissues, means for preventing such adhesion, and process for producing said means; Anthony N. de Belder, et al., 514/57, 54, 59, 60, 62; 536/55.1, 55.2, 56, 58, 106, 112 [IMAGE AVAILABLE]

US PAT NO: 4,886,787 [IMAGE AVAILABLE] L3: 33 of 55 DATE ISSUED: Dec. 12, 1989
TITLE: Method of preventing adhesion between body tissues, means for preventing such adhesion, and process for producing said means
INVENTOR: Anthony N. de Belder, Uppsala, Sweden
Thomas Malson, Uppsala, Sweden
ASSIGNEE: Pharmacia AB, Uppsala, Sweden (foreign corp.) APPL-NO: 06/847,171
DATE FILED: Jan. 23, 1986
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Elli Peselev
LEGAL-REP: Fred Philpitt

US PAT NO: 4,886,787 [IMAGE AVAILABLE] L3: 33 of 55

ABSTRACT:

The invention is concerned with a method of preventing adhesions or accretions of body tissues inter se by means of employing a degradable gel of a crosslinked carboxyl-containing polysaccharide. The invention also covers a gel product to be used for this purpose, and a process for preparing said product by means of crosslinking with a di- or polyfunctional epoxide at a pH of from 2 to 5.

34. 4,879,375, Nov. 7, 1989, Preparation of hyaluronic acid from synovial fluid; David Cullis-Hill, 536/55.1, 124 [IMAGE AVAILABLE]

US PAT NO: 4,879,375 [IMAGE AVAILABLE] L3: 34 of 55 DATE ISSUED: Nov. 7, 1989
TITLE: Preparation of hyaluronic acid from synovial fluid INVENTOR: David Cullis-Hill, 111 Bronte Road, Bondi Junction N.S.W., Australia, 2022
APPL-NO: 07/002,699
DATE FILED: Feb. 9, 1987
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
ASST-EXMR: Everett White
LEGAL-REP: Nixon & Vanderhye

US PAT NO: 4,879,375 [IMAGE AVAILABLE] L3: 34 of 55
ABSTRACT:

A method for preparing high purity **hyaluronic** acid comprising **treating** a proteinaceous solution containing **hyaluronic** acid to precipitate protein and said hyaluronic acid from the solution, denaturing the protein, adding the hyaluronic acid and denatured protein to a solution in which the hyaluronic acid is soluble, digesting the protein and recovering hyaluronic acid.

35. 4,851,521, Jul. 25, 1989, Esters of hyaluronic acid; Francesco della Valle, et al., 536/55.1; 424/423, 443, 489; 514/54, 844, 880 [IMAGE AVAILABLE]

US PAT NO: 4,851,521 [IMAGE AVAILABLE] L3: 35 of 55 DATE ISSUED: Jul. 25, 1989
TITLE: Esters of hyaluronic acid
INVENTOR: Francesco della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy
ASSIGNEE: Fidia, S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 06/881,454
DATE FILED: Jul. 2, 1986
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 4,851,521 [IMAGE AVAILABLE] L3: 35 of 55
ABSTRACT:

The invention concerns the esters of hyaluronic acid in which all or only a portion of the carboxylic groups of the acid are esterified, and the salts of the partial esters with metals or with pharmacologically acceptable organic bases. The compounds possess interesting and precious bioplastic and pharmaceutical properties and may be used in innumerable fields, including cosmetics, surgery and medicine. The invention also includes pharmaceutical preparations containing, as an active ingredient, one or more hyaluronic acid esters, or a salt thereof as described above, as well as medicaments containing: (1) a pharmacologically active substance or an association of pharmacologically active substances and (2) a carrying vehicle containing a total or partial ester of hyaluronic acid. The invention includes also various uses of the hyaluronic esters or of the above mentioned medicaments, such as in medicine, surgery or cosmetics. The invention also relates to a new procedure for the preparation of polysaccharide esters containing carboxylic groups, such as in particular the above mentioned hyaluronic acid esters.

36. 4,828,828, May 9, 1989, Method of treating degenerative joint disease by injection of meth(acrylamide) (co)-polymers; Seymour F. Trager, et al., 514/180, 772.4, 825 [IMAGE AVAILABLE]

US PAT NO: 4,828,828 [IMAGE AVAILABLE] L3: 36 of 55 DATE ISSUED: May 9, 1989
TITLE: Method of treating degenerative joint disease by injection of meth(acrylamide) (co)-polymers
INVENTOR: Seymour F. Trager, 14 Sherwood Dr., Plainview, NY 11803 Victoria S. Chylinski, 11 Peghouse Rise, Slad Road, Stroud, Glos., England
APPL-NO: 07/078,687
DATE FILED: Jul. 28, 1987
ART-UNIT: 155
PRIM-EXMR: Joseph L. Schofer

ASST-EXMR: Peter F. Kulkosky
LEGAL-REP: Fidelman & Wolfe

US PAT NO: 4,828,828 [IMAGE AVAILABLE] L3: 36 of 55
ABSTRACT:

A method for the treatment of degenerative joint disease in a mammal suffering therefrom which includes administration by injection of an effective amount of a pharmaceutical composition into the arthritically afflicted joints of the mammal thereby lubricating and cushioning the joints. The composition includes acrylamide or methacrylamide polymers or copolymers thereof having a molecular weight from about 1 to about 15 million and a pharmaceutically acceptable diluent.

37. 4,820,516, Apr. 11, 1989, Hyaluronidase; Roy T. Sawyer, et al., 424/94.62; 435/201; 514/912, 913 [IMAGE AVAILABLE]

US PAT NO: 4,820,516 [IMAGE AVAILABLE] L3: 37 of 55 DATE ISSUED: Apr. 11, 1989
TITLE: Hyaluronidase
INVENTOR: Roy T. Sawyer, Swansea, United Kingdom
Jeffrey Edwards, Swansea, United Kingdom
ASSIGNEE: Biopharm (UK) Limited, Swansea, United Kingdom (foreign corp.)
APPL-NO: 06/829,785
DATE FILED: Feb. 14, 1986
ART-UNIT: 183
PRIM-EXMR: John Rollins
LEGAL-REP: Bert J. Lewen, Henry Sternberg

US PAT NO: 4,820,516 [IMAGE AVAILABLE] L3: 37 of 55
ABSTRACT:

The hyaluronidase, which is a hyaluronic acid-specific endo-.beta.-glucuronidase, having a molecular weight of about 28,500 in non-reduced form, is derived from buffalo leeches (that is, leeches of the sub-family Hirudinariinae, such as the species Hirudinaria manillensis or Poecilobdella granulosa). The hyaluronidase, which cleaves hyaluronic acid, but not chondroitin, chondroitin -4- sulphate, chondroitin -6- sulphate or heparin, is considerably more stable at high temperatures and extremes of pH than known leech hyaluronidase. It has a wide range of uses where breakdown of hyaluronic acid is required; of particular interest is in pharmaceutical or veterinary formulations, either as an active agent or a spreading or percutaneous factor. The hyaluronidase is useful for stimulating flow of physiological fluids in the eye (for example, in the treatment of glaucoma).

38. 4,813,942, Mar. 21, 1989, Three step wound treatment method and dressing therefor; Oscar M. Alvarez, 602/49; 424/445, 448; 602/56; 604/304 [IMAGE AVAILABLE]

US PAT NO: 4,813,942 [IMAGE AVAILABLE] L3: 38 of 55 DATE ISSUED: Mar. 21, 1989
TITLE: Three step wound treatment method and dressing therefor INVENTOR: Oscar M. Alvarez, East Brunswick, NJ
ASSIGNEE: Bioderm, Inc., Plainsboro, NJ (U.S. corp.) APPL-NO: 07/026,950
DATE FILED: Mar. 17, 1987
ART-UNIT: 336
PRIM-EXMR: C. Fred Rosenbaum
ASST-EXMR: Mark O. Polutta
LEGAL-REP: Brumbaugh, Graves, Donohue & Raymond

US PAT NO: 4,813,942 [IMAGE AVAILABLE] L3: 38 of 55
ABSTRACT:

The invention provides a method of treating wounds in accordance with stages in the healing process by providing environments ideally suited to each stage of chronic wound repair. These environments are designed to improve cell and enzyme function. In the first phase of the treatment, the wound is treated with a debridement dressing which creates an acidic, hypoxic, warm and airtight environment. The debridement dressing comprises a hydrocolloid adhesive combination containing from about 35% to 50% pectin or other hydrocolloid or hydrophilic particle capable of reducing the pH, and further includes a means for monitoring the pH at the wound/dressing interface without removing the dressing. The second phase of the wound treatment is designed to enhance regeneration and provide natural protection against pathogenic invasion. The regeneration dressing used in this phase of treatment comprises a hydrocolloid adhesive containing 5% to 10% pectin to provide wet tack and 30% to 60% of a highly absorptive hydrocolloid or hydrophilic material such as sodium carboxymethylcellulose. The regenerative phase of the treatment yields a healed but fragile wound with thin epidermis which is prone to reinjury. Accordingly, the final phase of the treatment involves a protective dressing which promotes thickening of the epidermal cells, thus strengthening the healed wound. The protective dressing for use in this third phase contains 0.05% to 20% hyaluronic acid, preferably in a carrier or absorbent which will provide controlled delivery over a period of 24 to 96 hours.

39. 4,808,576, Feb. 28, 1989, Remote **administration** of **hyaluronic** acid to mammals; Richard H. Schultz, et al., 514/54, 825; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 4,808,576 [IMAGE AVAILABLE] L3: 39 of 55 DATE ISSUED: Feb. 28, 1989
TITLE: Remote **administration** of **hyaluronic** acid to mammals
INVENTOR: Richard H. Schultz, Lenexa, KS
Terry H. Wollen, Wellsville, KS
Nathan D. Greene, Leawood, KS
Karen K. Brown, Kansas City, MO
John O. Mozier, Stanley, KS

ASSIGNEE: Mobay Corporation, Pittsburgh, PA (U.S. corp.) APPL-NO: 06/856,732

DATE FILED: Apr. 28, 1986

ART-UNIT: 183

PRIM-EXMR: Ronald W. Griffin

LEGAL-REP: Gene Harsh, Joseph C. Gil, Lyndanne M. Whalen

US PAT NO: 4,808,576 [IMAGE AVAILABLE] L3: 39 of 55

ABSTRACT:

The present disclosure is concerned with the discovery that hyaluronic acid, an agent well known to reduce the sequelae of trauma in mammalian joint tissue when applied directly to the traumatized tissue, will be carried to such traumatized tissue by the mammal's natural processes if applied at a site remote from the traumatized tissue. Thus, hyaluronic acid, in any therapeutically acceptable form, can be administered by the typical remote routes including intravenous, intramuscular, subcutaneous and topical. This makes the utilization of hyaluronic acid much more convenient and attractive. For instance the treatment of arthritis in horse or human joints with hyaluronic acid no longer requires more difficult intra articular injections.

40. 4,801,619, Jan. 31, 1989, Hyaluronic acid preparation to be used for treating inflammations of skeletal joints; Gert T. Lindblad, 514/42, 54; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 4,801,619 [IMAGE AVAILABLE] L3: 40 of 55 DATE ISSUED: Jan. 31, 1989
TITLE: Hyaluronic acid preparation to be used for treating inflammations of skeletal joints
INVENTOR: Gert T. Lindblad, Upsala, Sweden
ASSIGNEE: Pharmacia AB, Upsala, Sweden (foreign corp.) APPL-NO: 06/934,410
DATE FILED: Nov. 4, 1986
ART-UNIT: 183
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Fred Philpitt

US PAT NO: 4,801,619 [IMAGE AVAILABLE] L3: 40 of 55

ABSTRACT:

Hyaluronic acid preparation containing an effective amount of hyaluronic acid of a molecular weight exceeding 3.times.10.sup.6 dalton, for intra-articular administration in the treatment of steroid arthropathy and progressive cartilage degeneration caused by proteoglycan degradation.

41. 4,784,991, Nov. 15, 1988, Heavy metal salts of hyaluronic acid and their use as antimicrobial agents; Abraham Nimrod, et al., 514/62; 424/65; 514/21, 495, 500 [IMAGE AVAILABLE]

US PAT NO: 4,784,991 [IMAGE AVAILABLE] L3: 41 of 55 DATE ISSUED: Nov. 15, 1988
TITLE: Heavy metal salts of hyaluronic acid and their use as antimicrobial agents
INVENTOR: Abraham Nimrod, Rehovot, Israel
Benjamin Greenman, Rehovot, Israel
ASSIGNEE: Bio-Technology General Corp., New York, NY (U.S. corp.) APPL-NO: 07/023,666
DATE FILED: Mar. 9, 1987
ART-UNIT: 134
PRIM-EXMR: Barry S. Richman
ASST-EXMR: T. J. Wallen
LEGAL-REP: John P. White

US PAT NO: 4,784,991 [IMAGE AVAILABLE] L3: 41 of 55

ABSTRACT:

Heavy metal salts of hyaluronic acid have been prepared. In particular, this invention is directed to silver, gold, cerium and tungsten salts of hyaluronic acid. These heavy metal salts of hyaluronic acid are useful as antimicrobial agents. Gold **hyaluronate** may also be used to **treat** arthritis.

This invention also concerns methods of making the silver salt of hyaluronic acid as well as compositions containing silver hyaluronate or gold hyaluronate.

The invention also concerns composition containing heavy metal salts having radioactively labelled hyaluronate moieties.

42. 4,784,990, Nov. 15, 1988, High molecular weight sodium hyaluronate; Abraham Nimrod, et al., 514/54; 435/101, 885; 514/847, 915; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 4,784,990 [IMAGE AVAILABLE] L3: 42 of 55 DATE ISSUED: Nov. 15, 1988
TITLE: High molecular weight sodium hyaluronate
INVENTOR: Abraham Nimrod, Rehovot, Israel
Benjamin Greenman, Rehovot, Israel
Dov Kanner, Rehovot, Israel
Moshe Landsberg, Petah Tikva, Israel
ASSIGNEE: Bio-Technology General Corporation, New York, NY (U.S. corp.)
APPL-NO: 06/692,692
DATE FILED: Jan. 18, 1985
ART-UNIT: 185
PRIM-EXMR: Elizabeth C. Weimar
LEGAL-REP: John P. White

US PAT NO: 4,784,990 [IMAGE AVAILABLE] L3: 42 of 55

ABSTRACT:

A novel mutant microorganism *Streptococcus zooepidemicus* HA-116 ATCC 39920, has been produced. The microorganism produces large amounts of high molecular weight hyaluronic acid. The invention provides a method of obtaining such microorganisms.

The invention also concerns a method of obtaining sodium hyaluronate which comprises growing with vigorous agitation a microorganism of the genus *Streptococcus* under appropriate conditions in a suitable nutrient medium containing a sugar component as a carbon source. The sugar component is present in a substantially constant concentration between 0.2 and 10 grams per liter. The medium has a substantially constant pH between about 6.0 and 7.5 and includes a substantially constant magnesium ion concentration above 0.05 grams per liter. The sodium hyaluronate excreted into the medium by the organism is purified using methods involving precipitation, redissolving and reprecipitating the hyaluronate. Composition of sodium hyaluronate which are characterized by an absence of pyrogenicity and skin irritation are obtained.

43. 4,780,414, Oct. 25, 1988, Method of producing high molecular weight sodium hyallronate by fermentation of streptococcus; Abraham Nimrod, et al., 435/101, 253.4, 803, 818, 885 [IMAGE AVAILABLE]

US PAT NO: 4,780,414 [IMAGE AVAILABLE] L3: 43 of 55 DATE ISSUED: Oct. 25, 1988
TITLE: Method of producing high molecular weight sodium hyallronate by fermentation of streptococcus
INVENTOR: Abraham Nimrod, Rehovot, Israel
Benjamin Greenman, Rehovot, Israel
Dov Kanner, Rehovot, Israel
Moshe Landsberg, Petah Tikva, Israel
Yaffa Beck, Gedera, Israel
ASSIGNEE: Bio-Technology General Corp., New York, NY (U.S. corp.) APPL-NO: 06/815,957
DATE FILED: Jan. 9, 1986
ART-UNIT: 185
PRIM-EXMR: Elizabeth Weimar
LEGAL-REP: John P. White

US PAT NO: 4,780,414 [IMAGE AVAILABLE] L3: 43 of 55

ABSTRACT:

A novel mutant microorganism *Streptococcus zooepidemicus* HA-116 ATCC 39920, has been produced. The microorganism produces large amounts of high molecular weight hyaluronic acid. The invention provides a method of obtaining such microorganisms.

The invention also concerns a method of obtaining sodium hyaluronate which comprises growing with vigorous agitation a microorganism of the genus *Streptococcus* under appropriate conditions in a suitable nutrient medium containing a sugar component as a carbon source. The sugar component is present in a substantially constant concentration between 0.2 and 10 grams per liter. The medium has a substantially constant pH between about 6.0 and 7.5 and includes a substantially constant magnesium ion concentration above 0.05 grams per liter. The sodium hyaluronate excreted into the medium by the organism is purified using methods involving precipitation, redissolving and reprecipitating the hyaluronate. Composition of sodium hyaluronate which are characterized by an absence of pyrogenicity and skin irritation are obtained.

44. 4,746,504, May 24, 1988, Heavy metal salts of hyaluronic acid and their use as antimicrobial agents; Abraham Nimrod, et al., 424/1.73, DIG.13; 514/54, 825, 914; 524/27, 29; 525/54.2; 536/4.1 [IMAGE AVAILABLE]

US PAT NO: 4,746,504 [IMAGE AVAILABLE] L3: 44 of 55 DATE ISSUED: May 24, 1988
TITLE: Heavy metal salts of hyaluronic acid and their use as antimicrobial agents
INVENTOR: Abraham Nimrod, Rehovot, Israel
Benjamin Greenman, Rehovot, Israel
ASSIGNEE: Bio-Technology General Corp., New York, NY (U.S. corp.) APPL-NO: 06/840,419
DATE FILED: Mar. 14, 1986
ART-UNIT: 134
PRIM-EXMR: Barry S. Richman
ASST-EXMR: T. J. Wallen
LEGAL-REP: John P. White

US PAT NO: 4,746,504 [IMAGE AVAILABLE] L3: 44 of 55

ABSTRACT:

Heavy metal salts of hyaluronic acid have been prepared. In particular, this invention is directed to silver, gold, cerium and tungsten salts of hyaluronic acid. These heavy metal salts of hyaluronic acid are useful as antimicrobial agents. Gold **hyaluronate** may also be used to **treat** arthritis. This invention also concerns methods of making the silver salt of hyaluronic acid as well as compositions containing silver hyaluronate or gold hyaluronate. The invention also concerns composition containing heavy metal salts having radioactively labelled hyaluronate moieties.

45. 4,736,024, Apr. 5, 1988, Process for preparing salt of hyaluronic acid with a pharmaceutically active substance; Francesco Della Valle, et al., 536/55.3, 18.7, 54, 55.2, 101, 121 [IMAGE AVAILABLE]

US PAT NO: 4,736,024 [IMAGE AVAILABLE] L3: 45 of 55 DATE ISSUED: Apr. 5, 1988
TITLE: Process for preparing salt of hyaluronic acid with a pharmaceutically active substance
INVENTOR: Francesco Della Valle, Padova, Italy
Aurelio Romeo, Rome, Italy
Silvana Lorenzi, Padova, Italy
ASSIGNEE: Fidia, S.p.A., Abano Terme, Italy (foreign corp.) APPL-NO: 06/847,632
DATE FILED: Apr. 3, 1986
ART-UNIT: 123
PRIM-EXMR: J. R. Brown
ASST-EXMR: Elli Peselve
LEGAL-REP: Birch, Stewart, Kolasch & Birch

US PAT NO: 4,736,024 [IMAGE AVAILABLE] L3: 45 of 55

ABSTRACT:

Pharmaceutical preparations for topical administration containing a pharmacologically active substance together with hyaluronic acid or a molecular weight fraction thereof. The hyaluronic acid may be in the form of the free acid or may be a salt with an alkali or alkaline earth metal, magnesium, aluminum or ammonium, or in the form of a salt with one or more pharmacologically active substances.

46. 4,725,585, Feb. 16, 1988, Method of enhancing the host defense; Per S. W. Wenge, et al., 514/54; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 4,725,585 [IMAGE AVAILABLE] L3: 46 of 55 DATE ISSUED: Feb. 16, 1988
TITLE: Method of enhancing the host defense
INVENTOR: Per S. W. Wenge, Upsala, Sweden
Lena D. Hakansson, Upsala, Sweden
Henning R. Hallgren, Balinge, Sweden
ASSIGNEE: Pharmacia AB, Upsala, Sweden (foreign corp.) APPL-NO: 06/778,560
DATE FILED: Sep. 20, 1985
ART-UNIT: 123
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Stiefel, Gross, Kurland & Pavane

US PAT NO: 4,725,585 [IMAGE AVAILABLE] L3: 46 of 55

ABSTRACT:

The invention relates to a method of enhancing or regulating the host defense of a mammal, said method comprising administering to a mammal a therapeutically effective amount of hyaluronic acid.

47. 4,713,448, Dec. 15, 1987, Chemically modified hyaluronic acid preparation and method of recovery thereof from animal tissues; Endre A. Balazs, et al., 536/55.1; 435/267 [IMAGE AVAILABLE]

US PAT NO: 4,713,448 [IMAGE AVAILABLE] L3: 47 of 55 DATE ISSUED: Dec. 15, 1987
TITLE: Chemically modified hyaluronic acid preparation and method of recovery thereof from animal tissues
INVENTOR: Endre A. Balazs, Ft. Lee, NJ
Adolf Leshchiner, Fairview, NJ
Adelya Leshchiner, Fairview, NJ
Philip Band, Brooklyn, NY
ASSIGNEE: Biomatix, Inc., Ridgefield, NJ (U.S. corp.) APPL-NO: 06/710,929
DATE FILED: Mar. 12, 1985
ART-UNIT: 123
PRIM-EXMR: Ronald W. Griffin
LEGAL-REP: Sheldon Palmer

US PAT NO: 4,713,448 [IMAGE AVAILABLE] L3: 47 of 55

ABSTRACT:

Disclosed is hylan, a chemically modified hyaluronic acid preparation characterized by the presence of small amounts (0.005-0.05% by weight) of aldehyde cross-linking groups covalently bonded to the hyaluronic acid molecular chains. Also disclosed is a method of obtaining hylan comprising **treating** **hyaluronic** acid in situ in animal tissues containing same with a treatment mixture including a reagent (typically an aldehyde) which is reactive towards hyaluronic acid and the proteins contained in the animal tissue.

48. 4,711,780, Dec. 8, 1987, Composition and process for promoting epithelial regeneration; Mostafa S. Fahim, 424/641; 514/562 [IMAGE AVAILABLE]

US PAT NO: 4,711,780 [IMAGE AVAILABLE] L3: 48 of 55 DATE ISSUED: Dec. 8, 1987
TITLE: Composition and process for promoting epithelial regeneration
INVENTOR: Mostafa S. Fahim, 500 Hulen Dr., Columbia, MO 65201 APPL-NO: 06/862,051
DATE FILED: May 12, 1986
ART-UNIT: 125
PRIM-EXMR: Leonard Schenkman
LEGAL-REP: Grace J. Fishel

US PAT NO: 4,711,780 [IMAGE AVAILABLE] L3: 48 of 55

ABSTRACT:

A medication for treating the surface epithelium is disclosed comprising vitamin C, a zinc salt and a sulfur amino acid. In some cases, the medication may additionally contain a mucopolysaccharide and/or a polysaccharide. A method of stimulating cell proliferation and new cell formation with said medication is also disclosed.

49. 4,703,108, Oct. 27, 1987, Biodegradable matrix and methods for producing same; Frederick A. Silver, et al., 530/356; 128/DIG.8; 424/94.64, 485; 514/801; 523/105, 111 [IMAGE AVAILABLE]

US PAT NO: 4,703,108 [IMAGE AVAILABLE] L3: 49 of 55 DATE ISSUED: Oct. 27, 1987
TITLE: Biodegradable matrix and methods for producing same INVENTOR: Frederick A. Silver, Long Valley, NJ
Richard A. Berg, Lambertville, NJ
David E. Birk, Somerset, NJ
Kevin Weadock, Piscataway, NJ
Conrad Whyne, Somerset, NJ
ASSIGNEE: University of Medicine & Dentistry of New Jersey, Newark, NJ (U.S. corp.)
APPL-NO: 06/843,828
DATE FILED: Mar. 26, 1986
ART-UNIT: 153
PRIM-EXMR: John Kight
ASST-EXMR: Nathan M. Nutter
LEGAL-REP: Weiser & Stapler

US PAT NO: 4,703,108 [IMAGE AVAILABLE] L3: 49 of 55

ABSTRACT:

There are disclosed processes for preparing biodegradable collagen-based matrices in sponge or sheet form wherein in one embodiment a collagen-based material including a collagen selected from the group consisting of types I, II and III collagens is freeze dried to form a collagen-based sponge which is contacted with a cross-linking agent selected from the group consisting of a carbodiimide or a succinimidyl active ester to form an intermediate collagen-based matrix which is subsequently subjected to conditions of severe dehydration to form the collagen-based matrix in sponge or sheet form. In another embodiment, a

collagen-based sponge or sheet is first subjected to conditions of severe dehydration followed by contacting the thus formed intermediate collagen-based matrix with a carbodiimide crosslinking compound to form the collagen-based matrix in sponge or sheet form. In still another embodiment of the present invention the cross-linking agent is admixed with the collagen-based material prior to formation of the collagen-based sponge or sheet followed by processing steps of severe dehydration. In a particularly preferred form of the invention, a carrier compound is incorporated during processing to form a collagen-based matrix in sponge or sheet form impregnated with a carrier compound wherein the carrier compound is selected from the group consisting of types IV and V collagen, fibronectin, laminin, hyaluronate, proteoglycan, epidermal growth factor, platelet derived growth factor, angiogenesis factor, antibiotic, antifungal agent, spermicidal agent, enzyme and enzyme inhibitor.

50. 4,517,295, May 14, 1985, Hyaluronic acid from bacterial culture; James W. Bracke, et al., 435/101, 801, 885; 536/55.1, 123 [IMAGE AVAILABLE]

US PAT NO: 4,517,295 [IMAGE AVAILABLE] L3: 50 of 55 DATE ISSUED: May 14, 1985
TITLE: Hyaluronic acid from bacterial culture
INVENTOR: James W. Bracke, Minnetonka, MN
Kipling Thacker, Minneapolis, MN
ASSIGNEE: Diagnostic, Inc., Minneapolis, MN (U.S. corp.) APPL-NO: 06/467,925
DATE FILED: Feb. 18, 1983
ART-UNIT: 127
PRIM-EXMR: Lionel M. Shapiro
LEGAL-REP: Schroeder, Siegfried, Vidas & Arrett

US PAT NO: 4,517,295 [IMAGE AVAILABLE] L3: 50 of 55

ABSTRACT:

Hyaluronic acid, a polysaccharide, is prepared in high yield from streptococcus bacteria by fermenting the bacteria under anaerobic conditions in a CO₂-enriched growth medium, separating the bacteria from the resulting broth and isolating the hyaluronic acid from the remaining constituents of the broth. The bacteria may be grown free of endotoxins by filtering all ingredients through a 10K Millipore.RTM. filter prior to inoculation of the medium and subsequently maintaining pyrogen-free conditions. Separation of the microorganisms from the polysaccharide is facilitated by killing the bacteria with trichloroacetic acid. After removal of the bacterial cells and concentration of the higher molecular weight fermentation products, the hyaluronic acid is isolated and purified by precipitation, resuspension and reprecipitation.

51. 4,500,676, Feb. 19, 1985, Hyaluronate modified polymeric articles; Endre A. Balazs, et al., 428/425.1; 8/115.61; 424/78.17, 78.27, 423; 427/400; 428/447, 452, 478.4, 481, 507; 524/29; 525/54.2, 54.22, 54.23 [IMAGE AVAILABLE]

US PAT NO: 4,500,676 [IMAGE AVAILABLE] L3: 51 of 55 DATE ISSUED: Feb. 19, 1985
TITLE: Hyaluronate modified polymeric articles
INVENTOR: Endre A. Balazs, Riverdale, NY
Adolf Leshchiner, Brooklyn, NY
ASSIGNEE: Biomatrix, Inc., Ridgefield, NJ (U.S. corp.) APPL-NO: 06/561,816
DATE FILED: Dec. 15, 1983
ART-UNIT: 155
PRIM-EXMR: Paul R. Michl
LEGAL-REP: Sheldon Palmer

US PAT NO: 4,500,676 [IMAGE AVAILABLE] L3: 51 of 55

ABSTRACT:

Polymeric materials (and articles made therefrom) including polyurethanes, polyesters, polyolefins, polyamides, polysiloxanes, vinylic and acrylic polymers are rendered biocompatible by including with the polymeric material hyaluronic acid or a salt thereof. The hyaluronic acid may be coated onto the surface of the polymeric material, dispersed throughout the body of the polymeric material, or both. The hyaluronic acid on the surface of the polymeric material may optionally be cross-linked. The biocompatible polymeric materials are used in the making of various prosthetic devices including heart valves, intraocular lenses, vascular grafts, pacemaker leads and the like.

52. 4,411,796, Oct. 25, 1983, Polyaminic resin for the selective separation of heparin from other glucosaminoglycans and method for the preparation thereof; Benito Casu, et al., 210/692; 127/46.2 [IMAGE AVAILABLE]

US PAT NO: 4,411,796 [IMAGE AVAILABLE] L3: 52 of 55 DATE ISSUED: Oct. 25, 1983
TITLE: Polyaminic resin for the selective separation of heparin from other glucosaminoglycans and method for the preparation thereof
INVENTOR: Benito Casu, Milan, Italy
Giangiacomo Torri, Bergamo, Italy

Giorgio Zoppetti, Milan, Italy

ASSIGNEE: Crinos Industria Farmabiologica, S.p.A., Villa Guardia, Italy (foreign corp.)
APPL-NO: 06/431,732
DATE FILED: Sep. 29, 1982
ART-UNIT: 143
PRIM-EXMR: Maurice J. Welsh
LEGAL-REP: Browdy & Neimark

US PAT NO: 4,411,796 [IMAGE AVAILABLE] L3: 52 of 55

ABSTRACT:

A novel polyaminic resin obtained by crosslinking a polyalkyleneamine (in particular polyethyleneamine) with diisocyanates in solution, is useful as a selective separation or extraction agent of a component having a "complementary" chemical structure (particularly heparin), by means of mere contact or "ionic exchange" with aqueous solutions containing it. Heparin is thus even quantitatively extracted from solutions containing it alone or in mixture with other glucosaminoglycans. The polyamine can then release the "adsorbed" heparin and be recovered by a treatment with saline solutions. The novel resin is used in pharmaco-biological fields.

53. 4,369,256, Jan. 18, 1983, Polyalkylene resins crosslinked with diisocyanate used for selective separation of heparin from other glucosaminoglycans; Benito Casu, et al., 521/25; 525/417; 528/68 [IMAGE AVAILABLE]

US PAT NO: 4,369,256 [IMAGE AVAILABLE] L3: 53 of 55 DATE ISSUED: Jan. 18, 1983
TITLE: Polyalkylene resins crosslinked with diisocyanate used for selective separation of heparin from other glucosaminoglycans
INVENTOR: Benito Casu, Milan, Italy
Giangiacomo Torri, Bergamo, Italy
Giorgio Zoppetti, Milan, Italy

ASSIGNEE: Crinos Industria Farmacobiologica S.p.A., Villa Guardia, Italy (foreign corp.)
APPL-NO: 06/251,874
DATE FILED: Apr. 6, 1981
ART-UNIT: 143
PRIM-EXMR: Maurice J. Welsh
LEGAL-REP: Browdy and Neimark

US PAT NO: 4,369,256 [IMAGE AVAILABLE] L3: 53 of 55

ABSTRACT:

A novel polyaminic resin obtained by crosslinking a polyalkyleneamine (in particular polyethyleneamine) with diisocyanates in solution, is useful as a selective separation or extraction agent of a component having a "complementary" chemical structure (particularly heparin), by means of mere contact or "ionic exchange" with aqueous solutions containing it. Heparin is thus even quantitatively extracted from solutions containing it alone or in mixture with other glucosaminoglycans. The polyamine can then release the "adsorbed" heparin and be recovered by a treatment with saline solutions. The novel resin is used in pharmaco-biological fields.

54. 4,272,522, Jun. 9, 1981, Method for stimulating phagocytic activity and synergistic compositions therefor; Endre A. Balazs, 424/94.61 [IMAGE AVAILABLE]

US PAT NO: 4,272,522 [IMAGE AVAILABLE] L3: 54 of 55 DATE ISSUED: Jun. 9, 1981
TITLE: Method for stimulating phagocytic activity and synergistic compositions therefor
INVENTOR: Endre A. Balazs, 3333 H. Hudson Pkwy., Riverdale, NY 10463 APPL-NO: 06/084,615
DATE FILED: Oct. 15, 1979
ART-UNIT: 121
PRIM-EXMR: Alan L. Rotman
LEGAL-REP: Sheldon Palmer, Peter L. Berger

US PAT NO: 4,272,522 [IMAGE AVAILABLE] L3: 54 of 55

ABSTRACT:

Phagocytosis is enhanced or stimulated by injection of a mixture of a soluble hyaluronic acid salt and muramidase in amounts sufficient to achieve a blood level of each in the range of 10-15 .mu.g/ml.

55. 4,141,973, Feb. 27, 1979, Ultrapure hyaluronic acid and the use thereof; Endre A. Balazs, 514/54, 769; 536/55.1 [IMAGE AVAILABLE]

US PAT NO: 4,141,973 [IMAGE AVAILABLE] L3: 55 of 55 DATE ISSUED: Feb. 27, 1979
TITLE: Ultrapure hyaluronic acid and the use thereof INVENTOR: Endre A. Balazs, Riverdale, NY
ASSIGNEE: Biotrics, Inc., Riverdale, NY (U.S. corp.) APPL-NO: 05/844,833
DATE FILED: Oct. 25, 1977
ART-UNIT: 125

PRIM-EXMR: Albert T. Meyers
ASST-EXMR: D. W. Robinson
LEGAL-REP: Hubbell, Cohen, Stiefel & Gross

US PAT NO: 4,141,973 [IMAGE AVAILABLE] L3: 55 of 55

ABSTRACT:

An ultra-pure, high molecular weight hyaluronic acid fraction which is characterized by the absence of significant cellular infiltration of the vitreous and anterior chamber, absence of significant flare in the aqueous humor, absence of significant haze or flare in the vitreous and absence of pathological changes to the cornea, lens, iris, retina, and choroid of the owl monkey eye when one milliliter of a 1% solution of the sodium salt thereof dissolved in physiological buffer is implanted in the vitreous replacing about one-half the existing liquid vitreous. This material is obtained from animal tissue containing hyaluronic acid by a process which comprises removing the blood from animal tissue containing hyaluronic acid, extracting hyaluronic acid therefrom, deproteinizing the hyaluronic acid extract, and removing any unidentified inflammation causing agents present therein by ****treating**** the deproteinized ****hyaluronic**** acid extract at a pH of 6.0 - 7.0 with a volume of chloroform at least about equal to that of the deproteinized extract, to form a two-phase mixture which is then stirred, sufficiently to ensure intimate contact between said two phases, at about 15.degree. - 40.degree. C., followed by separating out and discarding the chloroform phase.

fil
1